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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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PILLSBURY WINTHROP, LLP
P.O. BOX 10500
MCLEAN, VA 22102

EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	**PAPER NUMBER**
1644	33

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/435,992	Applicant(s) HANNA
	Examiner GAMBEL	Art Unit 1644

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 12/10/02, 4/7/03

2a)☐ This action is **FINAL**. 2b)☑ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 60, 65-69, 71-72, 80-99

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 60, 65-69, 71-72, 80-99

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☑ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☑ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 32.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☑ Other: COPY OF DECISION ON PETITION

PAPER NO. 33

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission, filed on 4/7/03 (Paper No. 30), has been entered

Applicant's amendment, filed 12/10/02 (Paper No. 26), has been entered.
Claims 61-64, 70 and 73-79 have been canceled. Claims 1-59 have been canceled previously.
Claims 60, 65-69, 71, 72 and 82-85 have been amended.
Claims 86-99 have been added.

Claims 60, 65-69, 71-72 and 80-99 are pending.

2. Applicant's comments concerning that the prior Office Actions are not directed to the elected invention does not appear to be consistent with a review of the previous elections and Office Actions of record.

However, given applicant's amended claims limiting the methods of treating B cell leukemia comprising the administration of anti-CD20 and anti-CD40L antibodies, pending claims 60, 65-69, 71-72 and 80-99 are under consideration in the instant application.

3. Applicant's provision of Figures 1-4 in conjunction with the Hariharan affidavit who attests to the fact that these Figures are the same Figures described in the as-filed application, filed 4/22/02 (Paper No. 20), has been acknowledged

Applicant's Request for Entry of Figures Representing the Results Described in the specification has been DISMISSED by the Office of Petitions, mailed 9/4/02 (Paper No. 25).

4. Claims 68, 82-83, 86-88, 93-99 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

It is apparent that Mab 24-31 and IDEC-C2B8 antibodies are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the pertinent cell lines / hybridomas which produce these antibodies. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

Applicant's amendment, filed 4/22/02 (Paper No. 20), relies upon the allowance of the humanized anti-CD40L antibody IDEC-131 in a copending application and on the commercial availability of RITUXAN as well as U.S. Patent Nos. 5,776,456 and 5,843,849.

Again, it is noted that certain of these antibodies are claimed in U.S. Patents (e.g. see art rejections below) which would be indicative, but not necessarily mean (see MPEP 2404.01) that the enablement of biological materials under 35 USC, 112, first paragraph, has been satisfied.

Applicant is required to indicate which antibodies are enabled accordingly and to satisfy the deposit of the biological materials for the others accordingly.

Applicant's amendment, filed 12/10/02 (Paper No. 26), which indicates reliance upon U.S. Patent No. 5,843,349 for the enablement of IDEC-C2B8 and upon U.S. Patent No. 6,001,358 for the enablement of Mab24-31 is acknowledged.

It is noted that the claims recited in U.S. Patent No. 5,843,349 provide for the anti-CD20 antibody produced by transfectoma TCAE 8, which has been accorded ATCC Deposit NO. ATCC 69119 and the murine anti-CD20 antibody secreted by a hybridoma identified by ATCC Deposit No. 11388, which, in turn, appears to provide the appropriate deposit requirements under 35 USC 112, first paragraph for the enablement of IDEC-C2B8.

For clarity, applicant is invited to verify that the recitation of "IDEC-C2B8" refers only to the deposited material recited in the patent claims of U.S. Patent No. 5,843,349.

It is noted that the claims recited in U.S. Patent No. 6,001,358 provide for the certain amino and nucleic acid sequences encoding the variable regions and not the entire immunoglobulin sequence of the anti-CD40L antibody Mab 24-31.

II is noted that the sequence of an entire immunoglobulin satisfies the biological deposit of said immunoglobulin. Note that satisfaction for the biological deposit of the specific MAb 24-31 antibody requires the disclosure and recitation of its entire amino acid sequence and not based upon partial sequences.

Therefore, applicant's reliance upon U.S. Patent No. 6,001,358 does not appear to provide for the appropriate deposit requirements under 35 USC 112, first paragraph for the enablement of Mab 24-31.

5. Claims 66 and 68 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 66 and 68 are indefinite in the recitation of "IDEC-C2B8" and "Mab 24-31" because their characteristics are not known. The use of these "designations" as the sole means of identifying the claimed antibodies renders the claims indefinite because these are merely laboratory designations which do not clearly define the claimed products, since different laboratories may use the same laboratory designations to define completely distinct cell lines .

If the recitation of "IDEC-C2B8" refers only to the deposited material recited in the patented claims of U.S. Patent No. 5,843,439, then this aspect of the rejection will be withdrawn.

Given that U.S. Patent No. 6,001,358 appears to disclose only variable region amino and nucleic acid sequences, then the recitation of "Mab 24-31" does not provide sufficient identification of the entire "Mab 24-31".

Claims 66 and 68 contain the trademark or trade name "IDEC -C2B8". Where a trademark or trade name is used in a claims as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 USC 112, second paragraph, See Ex parte Simpson, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark or the trade name "IDEC-C2B8" is used to identify or describe an antibody, and accordingly, the identification or the description is indefinite. The relationship between a trademark or tradename and the product it identifies may be uncertain and arbitrary. The formula or characteristics of the product may change from time to time and yet it may continue to be sold under the same trademark or tradename.

Applicant is required to indicate whether "IDEC-C2B8" is a trademark or tradename. If "IDEC-C2B8" is not a trademark or a tradename, then this rejection will be withdrawn.

Alternatively, amending the claims to recite the appropriate ATCC Accession Numbers would obviate this rejection

The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

Applicant arguments, filed 12/10/02 (Paper No. 26), have been fully considered but are not found convincing for the reasons set forth herein.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 60, 65-69, 71-72 and 80-99 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kaminski et al. (U.S. Patent No. 6,287,537) AND/OR Anderson et al. (U.S. Patent No. 5,843,439) in view of Smiers et al. (Br. J. Haematol. 93: 125-130, 1996), Schattner et al. (Blood 91: 2689-2697, 1998), Gruss et al. (Leukemia and Lymphoma 24: 393-422, 1997), Renard et al. (Blood 87: 5162-5170, 1996), Black et al. (U.S. Patent No. 6,001,358), Noelle et al. (U.S. Patent No. 5,747,037) in view of standard chemotherapeutic treatments, including combination therapy of leukemias known and practiced by the ordinary artisan at the time the invention was made, as acknowledged on pages 39-40 of the instant specification essentially for the reasons of record set forth in Paper Nos. 18/24/29.

Claims 60, 65-69, 71-72 and 80-99 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Kaminski et al. (U.S. Patent No. 6,287,537) AND/OR Anderson et al. (U.S. Patent No. 5,843,439) in view of Smiers et al. (Br. J. Haematol. 93: 125-130, 1996), Schattner et al. (Blood 91: 2689-2697, 1998), Gruss et al. (Leukemia and Lymphoma 24: 393-422, 1997), Renard et al. (Blood 87: 5162-5170, 1996), Black et al. (U.S. Patent No. 6,001,358), Noelle et al. (U.S. Patent No. 5,747,037) in view of standard chemotherapeutic treatments, including combination therapy of leukemias known and practiced by the ordinary artisan at the time the invention was made, as acknowledged on pages 39-40 of the instant specification essentially for the reasons of record set forth in Paper Nos. 18/24/29 and in further in view of Uhr et al. (U.S. Patent No. 5,686,072).

Applicant's arguments, filed 12/10/02 (Paper No. 26), have been fully considered but are not found convincing essentially for the reasons of record.

A review of applicant's arguments and the examiner's rebuttal of record can be found in Paper No. 24.

Once a prima facie case of obviousness has been made the burden of going further is shifted to applicant. In re Keller, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981). This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968). See MPEP 2145.

Applicant argues that the ordinary artisan would view that Kaminski et al. teaching away from using non-radiolabeled anti-CD20 antibodies to treat B cell malignancies.

In contrast to applicant's assertions; disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. See In re Susi USPQ 423 (CCPA 1971). A known or obvious composition does not patentable simply because it has been described as somewhat inferior to some other product for the same use. See In re Gurley 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). See MPEP 2123.

Here, the claims encompass the use of radiolabeled anti-CD20 antibodies, which are clearly taught by Kaminski et al.

Anderson et al. teach the very same IDEC-C2B8 anti-CD20 antibodies encompass by the instant claims.

Applicant argues that Anderson et al. do not suggest or disclose treating leukemia by administering anti-CD20 in combination with anti-CD40L antibodies.

In contrast to applicant's assertions that there was no suggestion or motivation to combine anti-CD20 and anti-CD40L antibodies to treat leukemias and that the teachings of the secondary references show that leukemia cells show considerable heterogeneity, the following of record is reiterated for applicant's convenience.

Smiers et al. teach that is was known at the time the invention was made that B cell leukemias expressed both CD20 and CD40 and leukemic cells proliferate in response to either CD20 or CD40 activation (see entire document, including Discussion).

Schattner et al. teach that CD40L is expressed on certain chronic lymphocytic leukemias and is important factor in CLL tumor growth as well as an important factor in the generation of pathologic antibody in some patients with CLL (see entire document, including Abstract and Discussion). Schattner et al. also teach that is was known at the time the invention was made that B cell leukemias expressed both CD20 and CD40 (see Abstract).

Gruss et al. teach that CD40 is expressed on B cell leukemias and that the CD40:CD40L pathway, including CD40L-expressing T cells, which are readily detectable around neoplastic B cells, enhance B cell activation and growth (see pages 404-405, B cell Lymphomas and Lymphoproliferative Disorders). It is noted that Gruss et al. teach the therapeutic use of recombinant CD40L rather than CD40L-specific antibodies as inhibitors of malignant B cell growth (page 404, column 1). While Gruss et al. disclose the art known formation of neutralizing anti-mouse antibodies as a limitation of antibody therapy, such limitations have been long addressed by the use of recombinant antibodies such as humanized antibodies, known and practiced in the art for a decade (also, see Noelle et al. and Black et al. herein).

Renard et al. teach autologous $CD4^+$ T cells isolated from leukemia patients were able to induce CD40-dependent proliferation of B cell leukemic blasts (see entire document, including the Abstract). Also, this proliferative response was inhibited by anti-CD40L antibody (see Results).

Therefore, the prior art of Schattner et al., Gruss et al. and Renard et al. taught the importance of CD40L-mediated interactions in B cell leukemia and clinical manifestation. Also as pointed out above, Gruss et al. does teach that CD40:CD40L interactions are par of cellular activation and neoplastic tumor cell growth which would be useful for the therapeutic management of $CD40^+$ tumors (see page 404, column 1).

Therefore, the prior art does provide motivation and expectation of success in combining antagonists of CD40:CD40L interactions in addition to targeting CD20 in the treatment of B cell malignancies, such as leukemia.

Applicant's arguments that it was unknown whether the combination of two unconjugated and non-radiolabeled antibodies would effectively inhibit growth or kill leukemic cells is not found convincing in view of the art and prosecution of record.

In addition, Uhr et al. Has been added to provide the teachings that appropriate therapeutic regiments for using antibodies or combination of antibody immunotoxins would be known to those of skill at the time the invention the invention was made in applying anti-B cell antibodies, including combination of anti-B cell antibodies to treat leukemia at the time the invention was made (see entire document, including column 6, paragraph 2 and columns 11-12). Here, Uhr et al. teach the use of combining two different anti-B cell antibodies, including anti-B cell immunotoxins in conjunction with other anti-cancer therapies such as radiotherapy and chemotherapy.

It is noted that the anti-B cell antibodies taught by Uhr et al. affect cell cycle, which, in turn, would be similar to the use of anti-CD20 or anti-CD40L antibodies which affect B cell or B cell leukemia cell proliferation.

Furthermore, as applicant has acknowledged and argued, the claims are not limited to non-radiolabeled antibodies. Applicant has asserted the instant claims encompass both radiolabled and non-radiolabeled anti-CD20 and anti-CD40L antibodies. Therefore, applicant is arguing for limitations not claimed. Clearly, the prior art provides for teaching, motivation and expectation of success in treating leukemia with radiolabeled anti-CD20 and anti-CD40L antibodies, including their combination with known chemotherapeutic treatments for leukemia by the ordinary artisan at the time the invention was made.

One of ordinary skill in the art at the time the invention was made would have been motivated to select radiolabeled CD20-specific antibodies, non-radiolabeled CD40L-specific antibodies and standard chemotherapeutic to treat B cell leukemia at the time the invention was made, given the teachings above. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

8. Claims 60, 65-69, 71-72 and 80-99 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over pending claims of copending applications USSN 09/772,938 . Given the election in the instant case, the conflicting claims may or may not be identical, depending upon the invention(s) elected in these copending applications. The claims are not patentably distinct from each other because they appear to read on the same or nearly the same reagents to treat the same or nearly the same leukemias and lymphomas.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's amendment, filed 12/10/02 (Paper No. 26), requests that this provisional rejection be held in abeyance

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
June 30, 2003